(12) UK Patent Application (19) GB (11) 2 110 085 A

(21) Application No 8137029
(22) Date of filing
8 Dec 1981
(30) Priority data
(31) 502887
(32) 9 Jun 1981
(33) Spain (ES)
(43) Application published
15 Jun 1983
(51) INT CL³ A61K 39/08
(52) Domestic classification
A5B 103 132 AC
C6Y 119
(58) Field of Search
No search possible
(71) Applicant
Laboratorios de Especialidades Farmaceuticas Centrum SA
(Spain)
Sagitario No 12 Alicante
Spain
(72) Inventors
Jose Ruiz Merino
Eliseo Quintanilla Almagro
(74) Agent and/or Address for Service
Barker and Brettell and Duncan
138 Hagley Road
Edgbaston
Birmingham B16 9PW

(54) An anti-tetanus vaccine

(57) An anti-tetanus vaccine, which may be administered under the tongue, is produced by a process which includes the steps of the purification of the tetanus micro organism to make it active as a vaccine, and the reconstitution of the purified tetanus micro organism with heated twice distilled water so that the micro organism conserves and retains all its immunising qualities, to make it orally absorbable.

GB 2 110 085 A

SPECIFICATION

An anti-tetanus vaccine

The present invention relates to a new process for producing anti-tetanus vaccine, possessing such characteristics and properties that it may be administered in a new way, that is by placing it under the tongue.

In particular, the invention relates to a new technique of obtaining anti-tetanus vaccine by specially treating the tetanus virus so that it becomes active, that is, it may be absorbed under the tongue. This special treatment, which will be described in more detail below, consists of a method of producing the said tetanus virus.

Various international organisations, and especially the Pasteur Institute, have sponsored separate world wide investigations to try and discover new ways of administering anti-tetanus vaccine, with the intention of eliminating the syringe method which has been used until now, and which may cause unwanted side-effects, such as reactions causing hypertension, necrosis, and neuroparalytic symptoms.

For these reasons, experiments have been carried out in laboratories, using animals, which have been given the tetanus virus, which has been previously treated (the treatment being a process of purification, stabilisation, filtration, and liquification) surprisingly, these experiments showed that the treated virus was orally absorbable in different groups of animals, producing immunising anti-bodies of more than 0.01 anti-toxic units.

On the other hand, tests were carried out on people, making absolutely certain that there was no virus present, using the new method of anti-tetanus inoculation, by placing the vaccine under the tongue. Out of the people given the vaccine, they were approximately 77.5% immunised, and at the same time, it was clear that there were no adverse side-effects. 1,074 people were tested in this way.

Taking all this into account, it may be said that the present invention provides a new method of administering the classic tetanus virus, which has been previously treated, and which eliminates any inconveniences and dangers associated with injections, such as reactions causing hypertension, necrosis and neuroparalytic symptoms, amongst other adverse effects.

Until now, anti-tetanus vaccine has only been given by injection which may give rise to unwanted side-effects as described in the previous paragraph.

The advantages of this invention, compared to the previous technique, are basically as follows:

1) Fewer adverse side-effects, which at the same time means no dangers such as those associated with injections, for example, hepatitis, and neurological disorders, amongst others.

2) The avoidance of localised problems, resulting from the special formula, which has led the Pasteur Institute to state that "aluminium salts which are often used in the formula for non-poisonous tetanus, have caused cancer in rats . . . . ."

3) The use of a new method of administration, namely placing the vaccine under the tongue, is more acceptable to people belonging to health authorities.

The present invention relates to a new method of producing anti-tetanus vaccine, which may be administered orally, and would basically involve the special treatment, or production, of the tetanus virus, to make it active, that is orally absorbable.

The tetanus virus used as a basic substance in the method of this invention is the same as that used in biological products by the World Health Organisation, and it must fulfil all the requirements set out in the W.H.O. Information Circular No. 30.

In particular, in the process of this invention, a tetanus virus may be used, containing approximately 25 F.L. (flocs) per drop, equivalent to approximately 500 F.L. per c.c.

The process of the invention is characterised by the following phases or stages:

a) Purification of the virus by the above-mentioned characteristics with the aim of producing a purified tetanus virus, which will be active as a vaccine, and

b) Reconstruction of the purified tetanus virus with heated twice distilled water, treated with sufficient conserving agents, but which would not affect either the virus nor its container to ensure that the virus conserves and retains all its immunising qualities to make it orally active.

One method of purificaton as used in the first stage of the process of the invention would be the use of separate Physical methods, such as filtration, liquification and so on.

The tetanus virus, having been treated according to the process of the invention, was subjected to the following tests of characterisation:

1) Identification test
2) Sterility test
3) Activity test
4) Test for content of catalysts
5) Innocuity test
6) Test for the content of an agent
7) Determination of the pH

All these tests are set out in Information Circular No. 30 of the World Health Organisation.

The process used to make the anti-tetanus vaccine active, according to the invention, has been tested in rabbits and guinea-pigs, as well as in other animals. 20 rabbits or guinea-pigs were given a drop of vaccine under the ton-

gue, containing 25 F.L. per drop (tetanus virus) and which had been treated according to the method of the invention. After 18–21 days, a 'booster' was administered in the same way, and at the end of a week, it was established, by taking blood samples, that the vaccine had been effective, and that in 80% of the animals, levels of anti-toxin were circulating in the blood more than 0.01 of international anti-toxin unts. This proves that 80% of the animals treated for the infection caused by *Clostridium Tetani* had been immunised.

When these same animals were given a 'booster' at the end of 6 months, immunising anti-bodies containing more than 0.01 anti-toxin units, were produced in 90% of the immunised animals. These figures are similar to those obtained by the inoculation of viruses by syringe, whether absorbed or not, which until now was the only method used for the prevention of tetanus, but at the same time, the oral method eliminates any unwanted side-effects connected with injections, which have already been mentioned.

Also, as has been previously stated, a group of 1,074 people were examined, or tested with the vaccine obtained according to the invention, and this was administered under the tongue, resulting in 77.5% immunisation of the people given the vaccine.

This sufficiently describes the nature of the invention as well as its method of realisation, but it must be said that the uses described herein may be modified as long as they do not alter the basic principle, which is recognised by the following Patent Claims.

CLAIMS

1. Process for the production of anti-tetanus vaccine, which may be administered under the tongue, in which the process includes the following steps:—

a) Purification of the tetanus virus, which makes it active as a vaccine; and

b) Reconstruction of the purified tetanus virus, with heated twice distilled water so that the virus conserves and retains all its immunising qualities, to make it orally absorbable.

2. Process according to Claim 1, in which the basic virus used is a tetanus virus containing approximately 25 F.L. per drop, equivalent to 500 F.L. per c.c.

3. Process according to the previous Claims, in which the purification technique used at stage a) is Physical, involving filtration and liquification.

4. Process according to the previous Claims, in which the twice distilled water used at stage b) contains conserving agents which will not alter the virus nor its container.

5. Process for the production of anti-tetanus vaccine which may be administered under the tongue substantially as described in this specification.

Printed for Her Majesty's Stationery Office
by Burgess & Son (Abingdon) Ltd.—1983.
Published at The Patent Office, 25 Southampton Buildings.
London, WC2A 1AY, from which copies may be obtained.